

MODIFIED CLAIMS

5 *Sub* 1. Nucleic acid, the sequence of which is selected from the group consisting of sequences SEQ ID n° 1 to SEQ ID n° 25, and a homologous nucleic acid sequence thereof.

10 2. Nucleic acid, the sequence of which is selected from the group consisting of exon sequences as identified in table 2, and a homologous nucleic acid sequence thereof.

3. Nucleic acid comprising the sequence as shown in SEQ ID n° 26, a homologous sequence thereof, or a sequence identical to SEQ ID n° 26, except for a one base deletion of the nucleotide 1578 as shown in SEQ ID N° 26.

15 4. Isolated oligophrenin 1 polypeptide substantially comprising the aminoacid sequence of SEQ ID n° 27, or a homologous amino acid sequence thereof.

5. Vector for cloning and/or expression comprising a nucleic acid sequence of any of claims 1 to 3.

20 6. Host cell transfected with a vector according to claim 5.

7. Nucleic acid, the sequence of which has at least 15 bases and specifically hybridizes with a nucleic acid sequence according to any of claims 1 to 2, under stringent conditions.

25 8. Nucleic acid, the sequence of which has at least 15 bases and specifically hybridizes with a nucleic acid sequence according to claim 3 under stringent conditions.

30 9. Nucleic acid of claim 7 or 8, the sequence of which is selected from the group consisting of the sequences identified in table 3 or the complementary sequences thereof, said sequences identified in table 3 consisting of:
- nucleotide n° 727 to 746 of SEQ ID n° 2

- nucleotide n° 958 to 977 of SEQ ID n° 2
- nucleotide n° 375 to 394 of SEQ ID n° 3
- nucleotide n° 504 to 523 of SEQ ID n° 3
- nucleotide n° 418 to 437 of SEQ ID n° 4
- nucleotide n° 551 to 570 of SEQ ID n° 4
- nucleotide n° 423 to 445 of SEQ ID n° 5
- nucleotide n° 553 to 574 of SEQ ID n° 5
- nucleotide n° 388 to 407 of SEQ ID n° 6
- nucleotide n° 540 to 559 of SEQ ID n° 6
- nucleotide n° 436 to 458 of SEQ ID n° 7
- nucleotide n° 584 to 603 of SEQ ID n° 7
- nucleotide n° 219 to 239 of SEQ ID n° 8
- nucleotide n° 363 to 381 of SEQ ID n° 8
- nucleotide n° 108 to 128 of SEQ ID n° 9
- nucleotide n° 336 to 355 of SEQ ID n° 9
- nucleotide n° 361 to 380 of SEQ ID n° 10
- nucleotide n° 492 to 511 of SEQ ID n° 10
- nucleotide n° 81 to 100 of SEQ ID n° 11
- nucleotide n° 223 to 242 of SEQ ID n° 11
- nucleotide n° 188 to 207 of SEQ ID n° 12
- nucleotide n° 300 to 319 of SEQ ID n° 12
- nucleotide n° 166 to 189 of SEQ ID n° 13
- nucleotide n° 259 to 278 of SEQ ID n° 13
- nucleotide n° 133 to 152 of SEQ ID n° 14
- nucleotide n° 250 to 269 of SEQ ID n° 14
- nucleotide n° 151 to 170 of SEQ ID n° 15
- nucleotide n° 293 to 315 of SEQ ID n° 15
- nucleotide n° 221 to 244 of SEQ ID n° 16
- nucleotide n° 363 to 382 of SEQ ID n° 16
- nucleotide n° 305 to 324 of SEQ ID n° 17
- nucleotide n° 438 to 457 of SEQ ID n° 17
- nucleotide n° 25 to 44 of SEQ ID n° 18
- nucleotide n° 218 to 237 of SEQ ID n° 18
- nucleotide n° 51 to 70 of SEQ ID n° 19

- nucleotide n° 252 to 271 of SEQ ID n° 19
- nucleotide n° 206 to 225 of SEQ ID n° 20
- nucleotide n° 383 to 402 of SEQ ID n° 20
- nucleotide n° 151 to 170 of SEQ ID n° 21
- nucleotide n° 511 to 530 of SEQ ID n° 21
- nucleotide n° 294 to 313 of SEQ ID n° 22
- nucleotide n° 496 to 515 of SEQ ID n° 22
- nucleotide n° 179 to 198 of SEQ ID n° 23
- nucleotide n° 271 to 291 of SEQ ID n° 23
- nucleotide n° 65 to 84 of SEQ ID n° 24
- nucleotide n° 165 to 184 of SEQ ID n° 24
- nucleotide n° 152 to 172 of SEQ ID n° 26
- nucleotide n° 586 to 606 of SEQ ID n° 26
- nucleotide n° 641 to 663 of SEQ ID n° 26

10. Method for producing a recombinant oligophrenin 1 polypeptide, wherein a host cell of claim 6 is cultured in conditions allowing the expression of a polypeptide according to claim 4.

11. Monoclonal or polyclonal antibodies, or fragments thereof, chimeric or immunoconjugate antibodies, which are capable of specifically recognizing a polypeptide according to claim 4.

12. Use of the antibodies of claim 11 for detecting or purifying a polypeptide according to claim 4 in a biological sample.

13. Use of a nucleic acid according to any of claims ~~1, 2, 3, 7, 8~~ and 9, for detecting an abnormality in the oligophrenin 1 gene or in the transcripts of the oligophrenin 1 gene.

14. Method of *in vitro* diagnosis of a neurological disorder associated with an abnormality in the oligophrenin 1 gene or in the transcripts of the oligophrenin 1 gene, wherein one or more mutation(s) is detected in any of the sequences of claims 1 to 3.

15. Method according to claim 14 wherein said mutation is a one base deletion of the nucleotide 1578 as shown in SEQ ID N° 26.

16. Method of *in vitro* diagnosis according to any of claims 14 or 15 comprising the steps of :

5 - contacting a biological sample containing DNA with specific oligonucleotides having a sequence as defined in claim 7, permitting the amplification of all or part of the oligophrenin 1 gene, the DNA contained in the sample having being rendered accessible, where appropriate, to hybridization, and under conditions permitting a hybridization of the oligonucleotides with the DNA
10 contained in the biological sample ;

- amplifying said DNA ;

- detecting the amplification products ;

15 - comparing the amplified products as obtained to the amplified products obtained with a normal control biological sample, and thereby detecting a possible abnormality in the oligophrenin 1 gene.

17. Method of *in vitro* diagnosis according to any of claims 14 or 15 comprising the steps of :

- producing cDNA from mRNA contained in a biological sample ;

20 - contacting said cDNA with specific oligonucleotides having a sequence as defined in claim 8, permitting the amplification of all or part of the transcript of the oligophrenin 1 gene, under conditions permitting a hybridization of the primers with said cDNA ;

- amplifying said cDNA ;

25 - detecting the amplification products ;

- comparing the amplified products as obtained to the amplified products obtained with a normal control biological sample, and thereby detecting a possible abnormality in the transcript of the oligophrenin 1 gene.

30 18. Pharmaceutical composition comprising a purified oligophrenin 1 polypeptide of claim 4 and/or a homologous polypeptide thereof, or an isolated

nucleic acid sequence encoding said polypeptide in association with a pharmaceutically acceptable carrier

19. Pharmaceutical composition comprising an anti-sense sequence as defined in claim 7 or 8 in association with a pharmaceutically acceptable carrier.

20. Pharmaceutical composition comprising an antibody according to claim 11.

21. Transgenic non-human mammal expressing an exogenous oligophrenin 1 protein as defined in claim 4, or being modified so as to overexpress a native oligophrenin 1 protein as defined in claim 4, or so as to express a non-functional oligophrenin 1 protein as defined in claim 4.

22. Method for screening drugs likely to act on the signaling pathway to which the oligophrenin 1 protein belongs, wherein said drugs are tested on transgenic non-human mammals, or cells in culture, that overexpress oligophrenin 1 protein as defined in claim 4 or express a native oligophrenin 1 protein as defined in claim 4 that has been rendered non-functional.

23. Drug selected by the method of claim 22.

24. Pharmaceutical composition containing a drug of claim 23 in association with a pharmaceutically acceptable carrier.

25. Method of preventing and/or treating neurological disorders resulting from defects in the oligophrenin 1 gene or in the oligophrenin 1 protein or in a homologous gene or protein thereof, which comprises administering to a subject in need of a such treatment an amount of a pharmaceutical composition of claim 18 or 24 effective to prevent and/or alleviate said neurological disorders.